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Case Report

Childhood Sarcoidosis mimicking Tuberculosis: A case report

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Abstract

Sarcoidosis is a rare multisystem chronic inflammatory disease in children. We present a case of a five-year-old child with clinical features mimicking several diseases, including tuberculosis. After failure of treatment based on the suspected diagnosis, an axillary lymph node biopsy showed noncaseating granulomas compatible with sarcoidosis and appropriate treatment was then started.

Keywords: Childhood sarcoidosis. Mimicking. Tuberculosis.

INTRODUCTION

Sarcoidosis is a multisystem chronic inflammatory disease that affects most organs, mainly the lungs. It rarely affects children, with an incidence of 1/100 000 in children aged 15 years or under and 0.06/100 000 in children under 4 years of age[1]. On histopathology, the classic findings are noncaseating granulomas[2], but early-onset (<5 years of age) sarcoidosis is usually characterized by the clinical triad of ocular, skin, and joint involvement without typical pulmonary disease[3]. The five stages of sarcoidosis, based on the extent of pulmonary involvement are: stage 0 (normal chest x-ray), stage I (hilar lymphadenopathy only), stage II (hilar lymphadenopathy and pulmonary infiltrates), stage III (pulmonary infiltrates without lymph node enlargement), and stage IV (advanced fibrosis without lymph node enlargement). Stages I and II are the most common[3].

The purpose of this paper was to present and discuss a case of childhood sarcoidosis in which diagnosis was difficult and the clinical features mimicked those of other diseases, such as juvenile idiopathic arthritis, pulmonary tuberculosis, (TB) and lymphoma.

CASE REPORT

We present the case of a 5-year-old girl from the Northeast of Brazil. She was the third child of a non-consanguineous marriage and her mother had a history of abortion. She was born by cesarean section with an uneventful pregnancy and delivery. She was admitted to the hospital at the age of 4 years because of seborrheic dermatitis, bacillus Calmette-Guérin (BCG) lymphadenitis, Blashkoid pigmentary changes (**Figure 1A**), disseminated nodes, and hepatomegaly. Furthermore, a history of fever and anemia since the first month of life was reported. Thus, she was admitted for diagnosis and investigation. Prophylactic antibiotics for immune deficiency were initiated with sulfamethoxazole and trimethoprim, although lymphocyte and immunoglobulin profiles were normal. During hospitalization, the patient had polyarticular arthritis, and the diagnostic hypothesis was juvenile idiopathic arthritis. The purified protein derivative (PPD) test result was 13 mm, oxidative burst by flow cytometry using dihydrorhodamine 123 was negative, glucose-6-phosphate dehydrogenase levels and hemoglobin electrophoresis were normal. A skin biopsy

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showed hyperkeratosis and acanthosis with chronic perivascular infiltrates, with no granuloma or collagen degradation. A chest X-ray showed perihilar opacities. The patient was diagnosed with TB and Rifampin, Isoniazid and Pyrazinamide (RIP) therapeutic regimen including 10 mg/kg/day of rifampin, 10 mg/kg/day of isoniazid, and 35 mg/kg/day of pyrazinamide was prescribed for the first 2 months and pyrazinamide was stopped in the following 4 months. The patient received a blood transfusion because of worsening anemia.

During outpatient follow-up, a colonoscopy was performed due to episodes of hematochezia and the results showed mild lymphoid hyperplasia. The abdominal ultrasonography (USG) showed enlarged hepatic hilar lymph nodes and normal retroperitoneal lymph nodes. An abdominal CT revealed mesogastric expansive lesions and adjacent enlarged lymph nodes (**Figure 1B**).

In 2017, the child was again hospitalized for 23 days due to persistently enlarged lymph nodes. Lymphoma was suspected and we continued to investigate for an abdominal tumor. Tests for acid-alcohol-resistant bacilli (AARB) and fungi were negative; chest CT scan showed confluent mediastinal and bilateral axillary lymphadenopathy. An abdominal CT showed enlarged lymph nodes at the mesenteric root, measuring 1.0 cm in the short axis and in the periaortic, internal and external iliac, and inguinal chains measuring up to 0.9 cm in the short axis. Hand, feet, and chest X-ray findings were normal. Laboratory tests showed a hemoglobin level of 11.3 g/dL, leukocyte count of 12 700/mm³, and platelet count of 465 mil/mm³. A right axillary lymph node biopsy detected chronic granulomatous lymphadenitis with a noncaseating epithelioid granuloma (**Figure 1C**).

Based on the lymph node biopsy and medical history, the girl was diagnosed with sarcoidosis and treatment with prednisolone 1.0 mg/kg/day was initiated for 3 months.

Thiabendazole syrup 25 mg/day was added for 21 days for prophylaxis of strongyloidiasis and isoniazid 10 mg/kg/day was prescribed for 90 days due to the previous PPD reaction.

The patient is currently asymptomatic and is not on any new medications.

DISCUSSION

It is important to highlight that pulmonary TB was the initial diagnosis since PPD was strongly reactive at the age of 2 years, symptoms were present for more than two weeks, and the patient did not get better with antibiotic therapy. Moreover, even though there was no history of contact with infected individuals, there were radiologic changes during the same period. According to the Brazilian National Ministry of Health Scoring System for the diagnosis of pulmonary TB in children, this child's score (>40 points) indicated a very likely diagnosis of TB[4].

Although 36% of childhood TB cases in Brazil show perihilar opacity[5], this is not the most common finding for this age group, which include hilar and/or paratracheal enlarged lymph nodes, pneumonia with radiologic changes, slow disease evolution, occasional mediastinal lymph node enlargement, or occasional cavities formed during disease evolution and diffuse nodular infiltrates, with a miliary pattern[6].

Additionally, PPD should be carefully interpreted in individuals who have a history of BCG vaccination, particularly during the first 2 years of life, because they commonly present with a midsized induration of 10 mm or more[6,7].

Thus, a strong reaction to the tuberculin skin test presented by the child should not have been interpreted as a sign of active TB.

This was confirmed because the patient did not improve after undergoing treatment for TB, and less than a year from the end of the treatment the child still showed diffuse lymph node enlargement with a negative PPD.

In light of this clinical presentation, we suspected disease recurrence, drug resistant *Mycobacterium tuberculosis*, or that the patient may not have had TB. The negative AARB and fungi tests, diffuse lymph node enlargement, and abdominal tumor discovered 4 years after the first hospitalization led

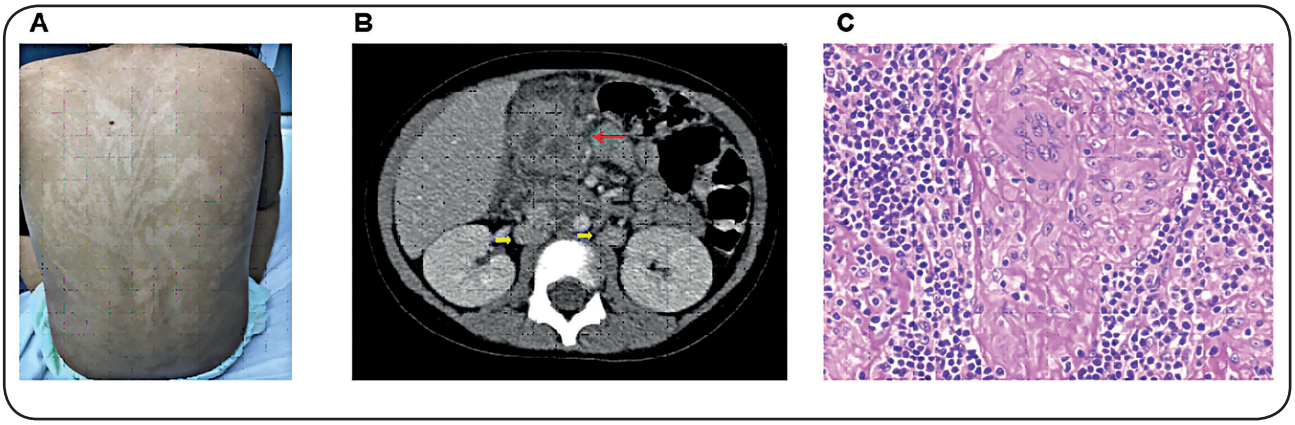

FIGURE 1: Changes in physical examination, abdominal Computed Tomography (CT) and lymph node biopsy images. (**A)** Colorless patches following Blashchko's lines in the torso. (**B)** Contrast enhanced upper abdomen CT scan (portal phase). The yellow arrows indicate a homogeneous retroperitoneal interaortocaval lymphadenopathy. The red arrow indicates a mesogastric mass with a necrotic/ liquefied center with densification of adjacent fatty tissue. (**C)** - Right axillary lymph node biopsy demonstrating characteristic noncaseating granuloma with lack of central necrosis, multinucleated giant cells with histiocytes and surrounding lymphocytes.

to a diagnostic hypothesis of lymphoproliferative disease. Histopathology of the axillar lymph nodes showed a noncaseating epithelioid granuloma, which finally determined the diagnosis as sarcoidosis.

The skin biopsy showed hyperkeratosis and acanthosis with chronic perivascular infiltrates, with no granuloma or collagen degradation, but this was not related to the underlying disease.

Even though there were several findings in common with other diseases, the authors believe that a diagnosis of sarcoidosis can be reached by exclusion of the other diagnoses and previous treatment failure.

Sarcoidosis diagnosis is always a challenge for pediatricians, as it is a disease that mimics other diseases, mainly the ones that present with granulomatous pulmonary impairment such as TB and histoplasmosis[8,9]. Furthermore, sarcoidosis may manifest with varying radiological features.

Unfortunately, knowledge about this disease in children is still incomplete and the majority of information is derived from studies on adults[10]. Moreover, the available epidemiological data is from European studies since data on Latin-American populations has not been updated, and therefore, the epidemiology of this condition in this continent has not been taken into consideration[11].

Currently the diagnosis of sarcoidosis is based on a combination of clinical features, radiological findings, and histological features. Therefore, outpatient follow-up is critical to eliminate other etiologies in the differential diagnosis and achieve an accurate diagnosis.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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